# STIC Search Report
## Biotech-Chem Library

STIC Database Tracking Number: 175065

**TO: Rei-Tsang Shiao**
**Location: rem/5A10/5C18**
**Art Unit: 1626**
**Tuesday, January 10, 2006**
**Case Serial Number: 10/757098**

**From: Barb O'Bryen**
**Location: Biotech-Chem Library**
**Remsen 1a69**
**Phone: 571-272-2518**

**barbara.obryen@uspto.gov**

## Search Notes

ACCESS DB # 175065

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DEC 27 2005
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**Scientific and Technical Information Center**

# SEARCH REQUEST FORM

Requester's Full Name: Robert (Reid-) Shiao Examiner #: 79521 Date: 12/27/05

Art Unit: 1626 Phone Number: 2-0707 Serial Number: 10/757,098

Location (Bldg/Room#): KEM (Mailbox #): 5A/96 Results Format Preferred (circle): PAPER DISK

**********

**To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:**

MEI

Title of Invention: phospholipid deriv of non-steroid

Inventors (please provide full names): Kaszk et al

Earliest Priority Date:

**Search Topic:**

***Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.***

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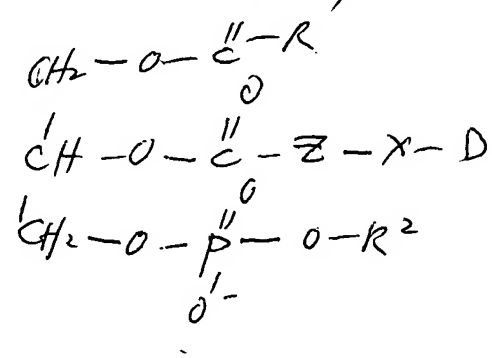
***For Sequence Searches Only*** ***Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.***

I. Search cpd I (see claim 1)



10. * $R^1$, [illegible] see sub
* $R^2$ is choline, ethanolamine, inositol, serine.
* Z is C
* X is N, S, C
* D is ibuprofen (see attachment)

II. methods of use of cpd I

**IN THE CLAIMS**

Please cancel claims 8, 18, 27 and 33 without prejudice.

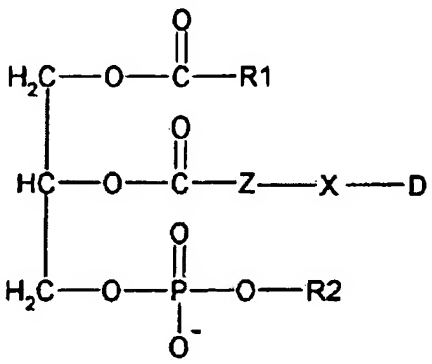
Please amend claims 1, 10, 11, 20 and 30 as indicated below.

Please withdraw claims 28-32 from consideration herein.

The listing of claims below will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A compound of the general formula I



Formula I

or a pharmaceutically acceptable salt thereof, wherein:

R1 is a saturated or unsaturated~~, substituted or unsubstituted~~ hydrocarbon chain having from 2 to 30 carbon atoms;

R2 is ~~H or~~ a phospholipid head group;

D is ~~the residue of a nonsteroidal anti-inflammatory drug having a functional group selected from the group consisting of carboxyl, hydroxyl, amine and thiol~~ ibuprofen, wherein D is attached through ~~said~~ a functional group to a bridging group, -C(O)-Z-X- , wherein Z is a saturated or unsaturated hydrocarbon chain having from 2 to 15 carbon atoms, and X is ~~selected from~~ an amino~~, hydroxy, thio and carbonyl groups, such that when the functional group of D is~~

~~carboxyl, X is selected from amino, hydroxy and thio, and when the functional group of D is amino, hydroxy or thio, X is a carbonyl~~ group.

2. (Previously Presented) The compound according to claim 1, wherein the conjugated residue of the nonsteroidal anti-inflammatory drug is pharmacologically inactive.

3. (Original) The compound according to claim 1, wherein an ester bond at position sn-2 of the phospholipid of the general formula I is cleaveable by a lipase.

4. (Original) The compound according to claim 3, wherein said lipase is a phospholipase.

5. (Original) The compound according to claim 4, wherein said phospholipase is phospholipase $A_2$ ($PLA_2$).

6. (Original) The compound according to claim 1, wherein R1 is an hydrocarbon chain having from 10 to 20 carbon atoms.

7. (Original) The compound according to claim 1, wherein R1 is an hydrocarbon chain having 15 or 17 carbon atoms.

8. (Canceled)

9. (Original) The compound according to claim 1, wherein R2 is selected from the group consisting of choline, ethanolamine, inositol and serine.

10. (Previously Presented) The compound according to claim 1 selected from the group consisting of:

~~1-Stearoyl-2-{3-[2-(2,6-dichloroanilino)phenylacetamido]propanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{4-[2-(2,6-dichloroanilino)phenylacetamido]butanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{5-[2-(2,6-dichloroanilino)phenylacetamido]valeroyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{6-[2-(2,6-dichloroanilino)phenylacetamido]hexanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{8-[2-(2,6-dichloroanilino)phenylacetamido]octanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{12-[2-(2,6-dichloroanilino)phenylacetamido]dodecanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{3-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]propanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{4-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]butanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{5-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]valeroyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{6-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]hexanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{8-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]octanoyl}-sn-glycero-3-phosphocholine,~~

1-Stearoyl-2-{3-[α-methyl-4-(2-methylpropyl)benzeneacetamido] propanoyl}-sn-glycero-3-phosphocholine, and

1-Stearoyl-2-{6-[α-methyl-4-(2-methylpropyl)benzeneacetamido] hexanoyl}-sn-glycero-3-phosphocholine~~,~~

~~1-Stearoyl-2-{3-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido]-propanoyl}-sn-glycero-3-phosphocholine,~~

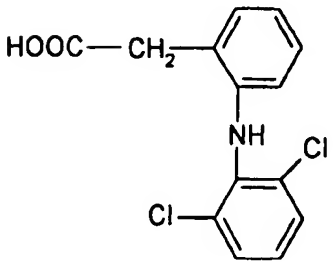
~~1-Stearoyl-2-{4-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido]-butanoyl}-sn-glycero-3-phosphocholine,~~

~~1-Stearoyl-2-{6-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido]-hexanoyl}-sn-glycero-3-phosphocholine, and~~

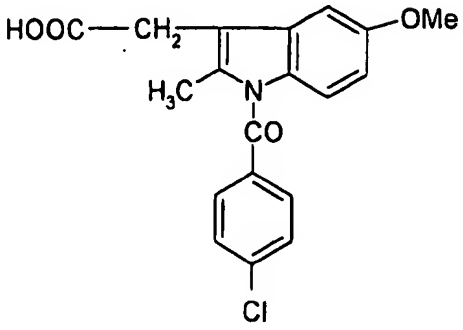
~~1-Stearoyl-2-{4-[2-(6-methoxynaphtyl)acetamido]butanoyl}-sn-glycero-3-phosphocholine~~.

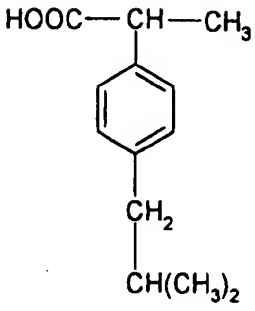
Wherein HOOC-$R_d$ in the synthesis scheme is a non-steroidal anti-inflammatory drug. For example, HOOC-$R_d$ may be selected from:

**Diclofenac**

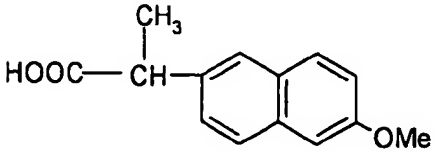



**Indomethacin**

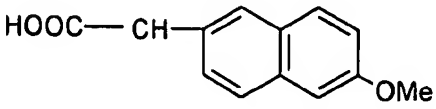



**Ibuprofen**




**Naproxen**




**6-Methoxy-2-naphthylacetic acid**

Chemical analysis: $C_{53}H_{83}N_3O_{11}PCl \cdot 2H_2O$.

Calculated: C 61.16%, H 8.46%, N 4.09%, P 3.03%, Cl 3.41%.

Found: C 61.21%, H 8.37%, N 4.04%, P 2.98%, Cl 3.47%.

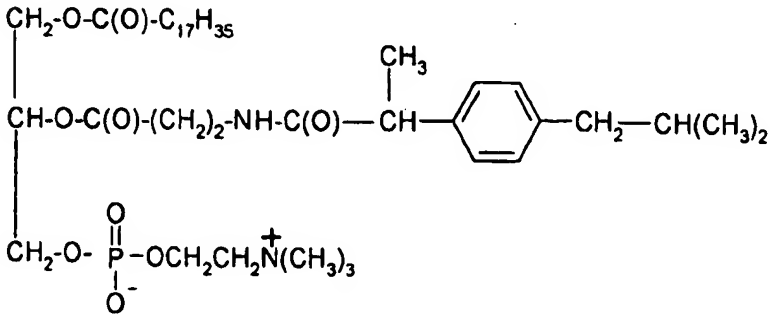
**EXAMPLE 3: Preparation of lipid derivatives of ibuprofen (DP-Ibu)**

The procedure for the preparation of lipid derivatives of ibuprofen (2-(4-isobutylphenyl)propionic acid) is the same as the process outlined in Example 1, steps 1 to 6, except that in step 6 instead of diclofenac the drug included in the reaction mixture is ibuprofen.

**Lipid derivatives of ibuprofen (DP-Ibu)**

The synthesized compounds were subjected to TLC analysis under the following conditions: Silica gel 60 on aluminum sheet. Eluent is chloroform:methanol:water (65:35:5, v/v). Indicator is a spray of the composition: 4-methoxybenzaldehyde (10 ml), absolute ethanol (200 ml), 98% sulfuric acid (10 ml) and glacial acetic acid (2 ml). The chromatogram is sprayed with the indicator and then charred at 100°C.

*1-Stearoyl-2-{3-[α-methyl-4-(2-methylpropyl)benzeneacetamido]propanoyl}-sn-glycero-3-phosphatidylcholine.*



White wax. Hygroscopic. Yield 60%.

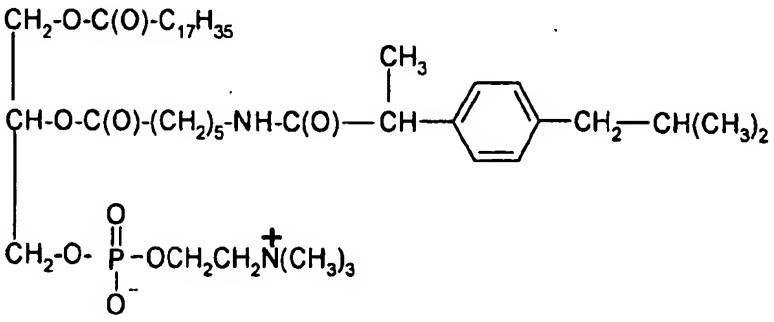
TLC analysis: One spot. $R_f$ is 0.38.

$^1$H NMR ($CD_3OD$), δ (ppm): 0.88-0.93 (m, 9H), 1.29 (s, 28H), 1.41-1.44 (d, 3H), 1.58-1.63 (m, 2H), 1.80-1.90 (m, 1H), 2.28-2.35 (t, 2H), 2.43-2.46 (d, 2H), 2.51-2.57 (t, 2H), 3.22 (s, 9H), 3.40-3.45 (m, 2H), 3.61-3.66 (m, 3H), 3.98-4.41 (several m, 6H), 5.18 (m, 1H), 7.01-7.07 (d, 2H), 7.22-7.26 (d, 2H).

$^{31}$P NMR ($CD_3OD$), δ (ppm): -0.20(s).

Chemical analysis: $C_{42}H_{75}N_2O_9P$. $4H_2O$. Calculated: C 59.02%, H 9.93%, N 3.28%, P 3.63%. Found: C 59.26%, H 9.64%, N 3.43%, P 3.65%.

*1-Stearoyl-2-{6-[α-methyl-4-(2-methylpropyl)benzeneacetamido]hexanoyl}-sn-glycero-3-phosphatidylcholine.*



White wax. Hygroscopic. Yield 50%.

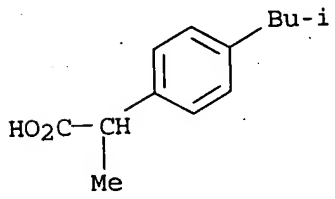
TLC analysis: One spot. $R_f$ is 0.38.

$^1$H NMR ($CD_3OD$), δ (ppm): 0.88-0.93 (m, 9H), 1.29 (broad s, 31H), 1.40-1.48 (m+d, 6H), 1.55-1.62 (m, 4H), 1.78-1.90 (m, 1H), 2.27-2.35 (m, 4H), 2.43-2.46 (d, 2H), 3.11-3.16 (m, 2H), 3.22 (s, 9H), 3.56-3.66 (m, 3H), 4.00-4.03 (t, 2H), 4.18-4.28 (several m, 4H), 5.18 (m, 1H), 7.07-7.11 (d, 2H), 7.22-7.25 (d, 2H).

$^{31}$P NMR ($CD_3OD$), δ (ppm): -0.20(s).

Chemical analysis: $C_{45}H_{81}N_2O_9P$. $2.5H_2O$. Calculated: C 62.07%, H 9.89%, N 3.22%, P 3.56%. Found: C 62.00%, H 10.01%, N 3.32%, P 3.19%.

CN Bruflam
CN Brufort
CN Buburone
CN Buluofen
CN Burana
CN Butacortelone
CN Butylenin
CN Carol
CN **Ibuprofen**
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
FS 3D CONCORD
DR 58560-75-1, 139466-08-3
MF C13 H18 O2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DIPPR*, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PATDPASPC, PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH, SPECINFO, SYNTHLINE, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

7974 REFERENCES IN FILE CA (1907 TO DATE)
236 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7994 REFERENCES IN FILE CAPLUS (1907 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> s ketoprofen/cn
L7 1 KETOPROFEN/CN

=> d

L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 22071-15-4 REGISTRY
ED Entered STN: 16 Nov 1984
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Hydratropic acid, m-benzoyl- (8CI)
OTHER NAMES:
CN (±)-2-(3-Benzoylphenyl)propionic acid
CN (±)-3-Benzoyl-α-methylbenzeneacetic acid
CN (±)-Ketoprofen
CN (±)-m-Benzoylhydratropic acid
CN (RS)-Ketoprofen

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Bib Data Sheet

**CONFIRMATION NO. 3472**

| SERIAL NUMBER | FILING DATE | CLASS | GROUP ART UNIT | ATTORNEY DOCKET NO. |
|---|---|---|---|---|
| 10/757,098 | 01/14/2004<br>RULE | 514 | 1626 | 800.1012DIV |

APPLICANTS

Alexander Kozak, Rehovot, ISRAEL;

Israel Shapiro, Ramla, ISRAEL;

** CONTINUING DATA **********

This application is a DIV of 09/856,009 05/16/2001 PAT 6,730,696 *
which is a 371 of PCT/IL99/00623 11/18/1999
(*)Data provided by applicant is not consistent with PTO records.

** FOREIGN APPLICATIONS **********

ISRAEL 127143 11/18/1998

Filed in 2/856,009 RK

IF REQUIRED, FOREIGN FILING LICENSE GRANTED ** SMALL ENTITY **
** 04/16/2004

| Foreign Priority claimed | STATE OR | SHEETS | TOTAL | INDEPENDENT |
|---|---|---|---|---|
| 35 USC 119 (a-d) conditions met | COUNTRY | DRAWING | CLAIMS | CLAIMS |
| Verified and Acknowledged | ISRAEL | 4 | 33 | 3 |

☒ yes ☐ no
☒ yes ☐ no ☒ Met after Allowance
Examiner's Signature Initials

ADDRESS
23280
DAVIDSON, DAVIDSON & KAPPEL, LLC
485 SEVENTH AVENUE, 14TH FLOOR
NEW YORK , NY
10018

TITLE
Phospholipid derivatives of non-steroidal anti-inflammatory drugs

| FILING FEE | FEES: Authority has been given in Paper | ☐ All Fees<br>☐ 1.16 Fees ( Filing )<br>☐ 1.17 Fees ( Processing Ext. of |
|---|---|---|

# STIC SEARCH RESULTS FEEDBACK FORM

## Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact***:

**Mary Hale, Information Branch Supervisor**
**Remsen Bldg. 01 D86**
**571-272-2507**

## Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

*Types of relevant prior art found:*

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

- *Relevant prior art **not found**:*
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

**Comments:**

**Drop off or send completed forms to STIC-Biotech-Chem Library Remsen Bldg.**

=> fil reg; d stat que l5; fil capl uspatf toxcenter; s l5; fil marpat; d stat que l8
FILE 'REGISTRY' ENTERED AT 16:21:00 ON 10 JAN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 9 JAN 2006 HIGHEST RN 871542-42-6
DICTIONARY FILE UPDATES: 9 JAN 2006 HIGHEST RN 871542-42-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

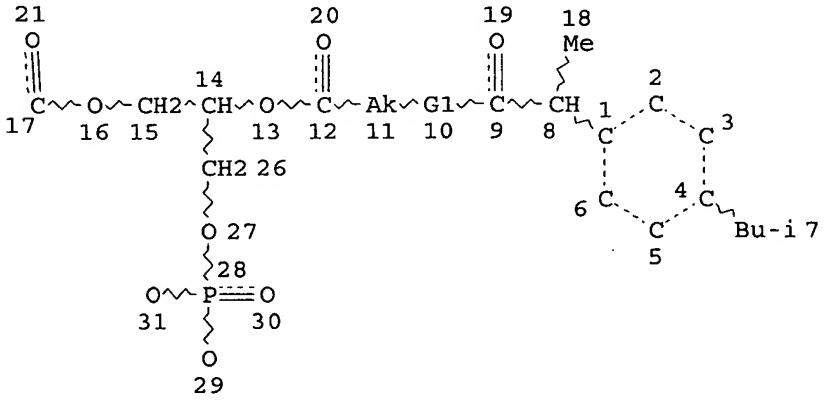
**********
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
**********

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

L1 STR

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 27

STEREO ATTRIBUTES: NONE
L5 2 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 19 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

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L9 4 L5

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FILE CONTENT: 1988-PRESENT (VOL 144 ISS 1 (20060101/ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 6949561 27 SEP 2005
DE 1020040544 15 SEP 2005
EP 1582199 05 OCT 2005
JP 2005320486 17 OCT 2005
WO 2005110983 24 NOV 2005

Expanded G-group definition display now available.

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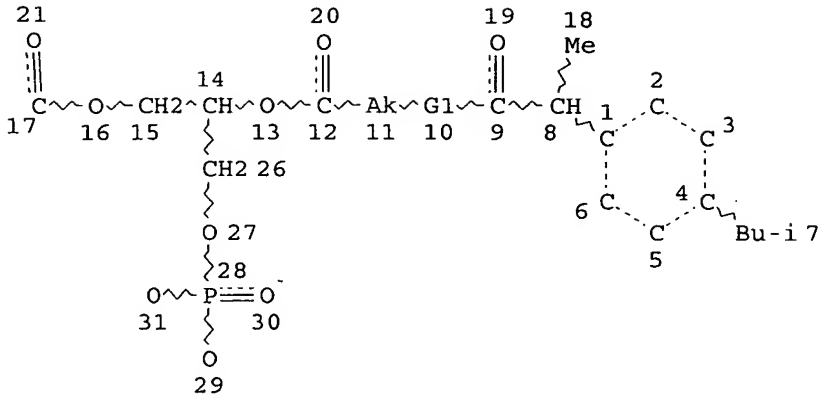
L6 STR



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MLEVEL IS CLASS AT 11
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 27

STEREO ATTRIBUTES: NONE
L8 1 SEA FILE=MARPAT SSS FUL L6

100.0% PROCESSED 1685 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.05

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PROCESSING COMPLETED FOR L9
PROCESSING COMPLETED FOR L8
L10 3 DUP REM L9 L8 (2 DUPLICATES REMOVED)
ANSWER '1' FROM FILE CAPLUS
ANSWERS '2-3' FROM FILE USPATFULL

— these are all the references to your compound - no sense in further narrowing with "method of using"

=> d ibib ed abs hitstr 1-3

L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2000:368364 CAPLUS
DOCUMENT NUMBER: 133:12744
TITLE: Phospholipid derivatives of nonsteroidal antiinflammatory drugs
INVENTOR(S): Kozak, Alexander; Shapiro, Israel
PATENT ASSIGNEE(S): D-Pharm Ltd., Israel
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000031083 | A1 | 20000602 | WO 1999-IL623 | 19991118 |
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| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2346869 | AA | 20000602 | CA 1999-2346869 | 19991118 |
| EP 1131326 | A1 | 20010912 | EP 1999-956297 | 19991118 |
| EP 1131326 | B1 | 20030507 | | |
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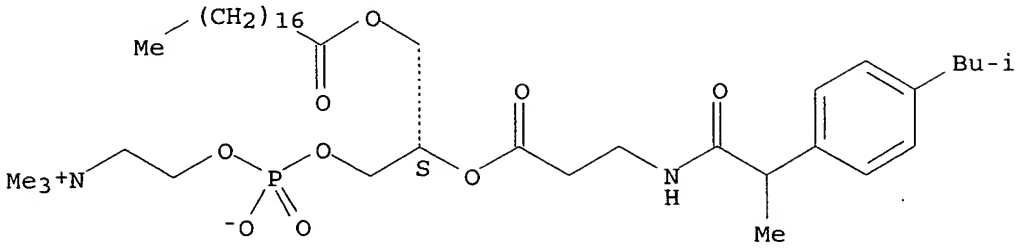
| JP 2002530410 | T2 | 20020917 | JP 2000-583911 | 19991118 |
| NZ 510938 | A | 20021126 | NZ 1999-510938 | 19991118 |
| AT 239739 | E | 20030515 | AT 1999-956297 | 19991118 |
| AU 766045 | B2 | 20031009 | AU 2000-12928 | 19991118 |
| IL 142683 | A1 | 20040620 | IL 1999-142683 | 19991118 |
| ZA 2001002718 | A | 20011005 | ZA 2001-2718 | 20010403 |
| US 6730696 | B1 | 20040504 | US 2001-856009 | 20010516 |
| US 2004147485 | A1 | 20040729 | US 2004-757098 | 20040114 |

PRIORITY APPLN. INFO.:
IL 1998-127143 A 19981119
WO 1999-IL623 W 19991118
US 2001-856009 A3 20010516

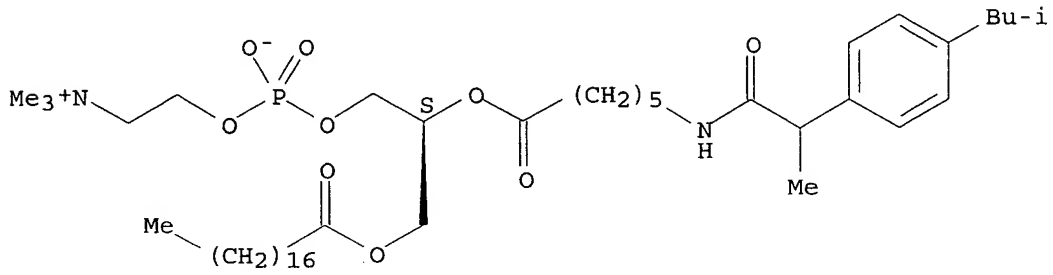
OTHER SOURCE(S): MARPAT 133:12744
ED Entered STN: 04 Jun 2000
AB The invention discloses compds. comprising nonsteroidal antiinflammatory drugs (NSAIDs) covalently linked to a phospholipid moiety via a bridging group. The invention further discloses a process for the synthesis of the compds., pharmaceutical compns. comprising them, and their use for the treatment of diseases and disorders related to inflammatory conditions.
IT **271781-47-6P 271781-48-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NSAID-phospholipid conjugate preparation, pharmaceutical compns. and therapeutic use)
RN 271781-47-6 CAPLUS
CN β-Alanine, N-[2-[4-(2-methylpropyl)phenyl]-1-oxopropyl]-, (1S)-4-hydroxy-8,8-dimethyl-4-oxido-1-[[(1-oxooctadecyl)oxy]methyl]-3,5-dioxa-8-azonia-4-phosphanon-1-yl ester, inner salt, (7S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 271781-48-7 CAPLUS
CN 3,5,8-Trioxa-15-aza-4-phosphaoctadecan-1-aminium, 4-hydroxy-N,N,N-trimethyl-17-[4-(2-methylpropyl)phenyl]-9,16-dioxo-7-[[(1-oxooctadecyl)oxy]methyl]-, inner salt, 4-oxide, (7S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 3 USPATFULL on STN
ACCESSION NUMBER: 2004:190712 USPATFULL
TITLE: Phospholipid derivatives of non-steroidal anti-inflammatory drugs
INVENTOR(S): Kozak, Alexander, Rehovot, ISRAEL
Shapiro, Israel, Ramla, ISRAEL
PATENT ASSIGNEE(S): D-Pharm, Ltd., Rehovot, ISRAEL (non-U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2004147485 | A1 | 20040729 |
| APPLICATION INFO.: | US 2004-757098 | A1 | 20040114 (10) |

RELATED APPLN. INFO.: Division of Ser. No. US 2001-856009, filed on 16 May 2001, GRANTED, Pat. No. US 6730696 A 371 of International Ser. No. WO 1999-IL623, filed on 18 Nov 1999, PENDING

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | IL 1998-127143 | 19981118 |

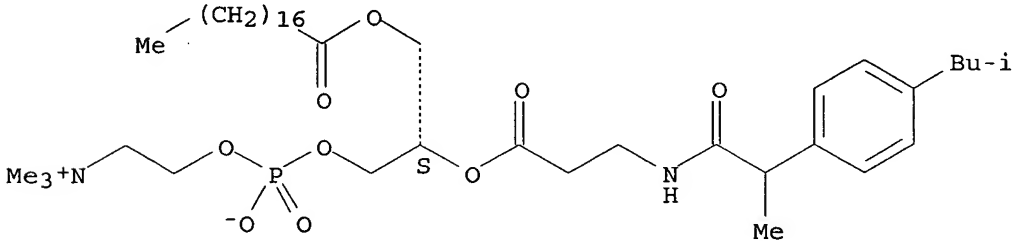
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: DAVIDSON, DAVIDSON & KAPPEL, LLC, 485 SEVENTH AVENUE,

14TH FLOOR, NEW YORK, NY, 10018
NUMBER OF CLAIMS: 33
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 1858
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are compounds having non-steroidal anti-inflammatory drugs (NSAIDS) covalently linked to a phospholipid moiety via a bridging group. Also disclosed are a process for the synthesis of the compounds, pharmaceutical compositions comprising the compounds and the use thereof for the treatment of diseases and disorders related to inflammatory conditions, such as the treatment of ischemia.

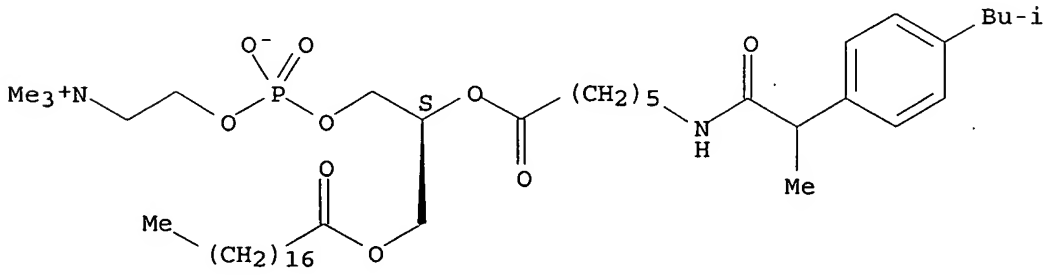
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **271781-47-6P 271781-48-7P**
(NSAID-phospholipid conjugate preparation, pharmaceutical compns. and therapeutic use)
RN 271781-47-6 USPATFULL
CN β-Alanine, N-[2-[4-(2-methylpropyl)phenyl]-1-oxopropyl]-, (1S)-4-hydroxy-8,8-dimethyl-4-oxido-1-[[(1-oxooctadecyl)oxy]methyl]-3,5-dioxa-8-azonia-4-phosphanon-1-yl ester, inner salt, (7S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 271781-48-7 USPATFULL
CN 3,5,8-Trioxa-15-aza-4-phosphaoctadecan-1-aminium, 4-hydroxy-N,N,N-trimethyl-17-[4-(2-methylpropyl)phenyl]-9,16-dioxo-7-[[(1-oxooctadecyl)oxy]methyl]-, inner salt, 4-oxide, (7S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 3 OF 3 USPATFULL on STN
ACCESSION NUMBER: 2004:109956 USPATFULL
TITLE: Phospholipid derivatives of non-steroidal

anti-inflammatory drugs

INVENTOR(S): Kozak, Alexander, Rehovot, ISRAEL
Shapiro, Israel, Ramla, ISRAEL

PATENT ASSIGNEE(S): D-Pharm, Ltd., Rehovot, ISRAEL (non-U.S. corporation)

| | NUMBER | KIND | DATE | |
|---|---|---|---|---|
| PATENT INFORMATION: | US 6730696 | B1 | 20040504 | |
| | WO 2000031083 | | 20000602 | |
| APPLICATION INFO.: | US 2001-856009 | | 20010516 | (9) |
| | WO 1999-IL623 | | 19991118 | |

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | IL 1998-127143 | 19981119 |

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: McKane, Joseph K.
ASSISTANT EXAMINER: Wright, Sonya
LEGAL REPRESENTATIVE: Davidson, Davidson & Kappel, LLC
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 1796
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are compounds having non-steroidal anti-inflammatory drugs (NSAIDS) covalently linked to a phospholipid moiety via a bridging group. Also disclosed are a process for the synthesis of the compounds, pharmaceutical compositions comprising the compounds and the use thereof for the treatment of diseases and disorders related to inflammatory conditions, such as the treatment of ischemia.

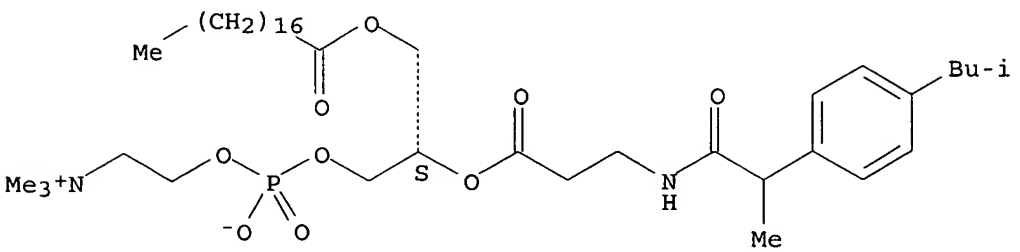
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **271781-47-6P 271781-48-7P**
(NSAID-phospholipid conjugate preparation, pharmaceutical compns. and therapeutic use)

RN 271781-47-6 USPATFULL

CN β-Alanine, N-[2-[4-(2-methylpropyl)phenyl]-1-oxopropyl]-, (1S)-4-hydroxy-8,8-dimethyl-4-oxido-1-[[(1-oxooctadecyl)oxy]methyl]-3,5-dioxa-8-azonia-4-phosphanon-1-yl ester, inner salt, (7S)- (9CI) (CA INDEX NAME)

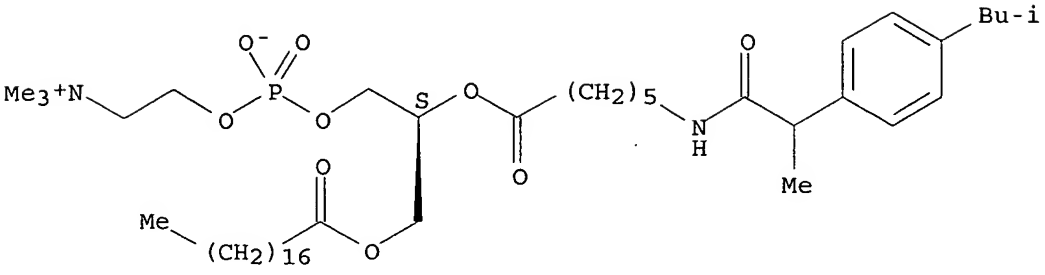
Absolute stereochemistry.




RN 271781-48-7 USPATFULL

CN 3,5,8-Trioxa-15-aza-4-phosphaoctadecan-1-aminium, 4-hydroxy-N,N,N-trimethyl-17-[4-(2-methylpropyl)phenyl]-9,16-dioxo-7-[[(1-oxooctadecyl)oxy]methyl]-, inner salt, 4-oxide, (7S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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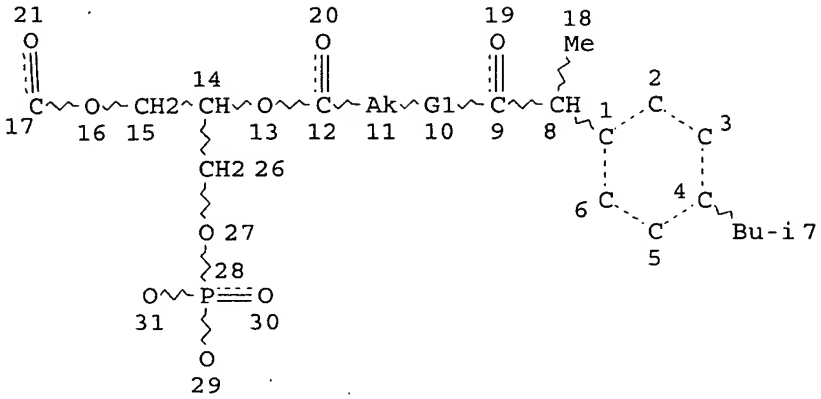


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MLEVEL  IS CLASS  AT  11
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  27

STEREO ATTRIBUTES: NONE
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SEARCH TIME: 00.00.05


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Searched by Barb O'Bryen, STIC 2-2518